



Spectroscopy Society of Pittsburgh

February Meeting

Wednesday – February 19, 2014

Duquesne University



5:30 PM	Technology Forum Speaker's Presentation - Wolfe Lecture Hall located in Bayer Hall
5:30 to 6:30PM	Social Hour - City View Café (6th Floor of Union)
6:30PM	Dinner - City View Café (6th Floor of Union)
8:00PM	Business Meeting– Laura Falk Hall located in Mellon Hall
8:15PM	Technical Program Speaker's Presentation– Laura Falk Hall

Deadline for Dinner Reservations 2/13/14 at NOON

[On-line Reservations](#)

TECHNICAL PROGRAM - 8:15 PM

Dr. Angela Gronenborn, University of Pittsburgh School of Medicine

"Synergy between NMR, cryo-EM and large-scale MD simulations - Novel Findings for HIV Capsid Function"



Mature HIV-1 particles contain a conical-shaped capsid that encloses the viral RNA genome and performs essential functions in the virus life cycle. Previous structural analysis of two- and three-dimensional arrays provided a molecular model of the capsid protein (CA) hexamer and revealed three interfaces in the lattice. Using the high-resolution NMR structure of the CA C-terminal domain (CTD) dimer and in particular the unique interface identified, it was possible to reconstruct a model for a tubular assembly of CA protein that fit extremely well into the cryoEM density map. A novel CTD-CTD interface at the local three-fold axis in the cryoEM map was confirmed by mutagenesis to be essential for function. More recently, the cryo-EM structure of the tube was solved at 8Å resolution and this cryo-EM structure allowed unambiguous modeling and refinement by large-scale molecular dynamics (MD) simulation, resulting in all-atom models for the hexamer-of-hexamer and pentamer-of-hexamer elements of spheroidal capsids. Furthermore, the 3D structure of a native HIV-

1 core was determined by cryo-electron tomography (Cryo-ET), which in combination with MD simulations permitted the construction of a realistic all-atom model for the entire capsid, based on the 3D authentic core structure.

Dr. Angela Gronenborn is one of the country's leading structural biologists and an internationally renowned specialist in the application of nuclear magnetic resonance (NMR) spectroscopy for investigating structure, dynamics and folding of biological macromolecules. She joined the faculty of the University of Pittsburgh as a Professor in the School of Medicine in 2004. In 2005, the Department of Structural Biology was established with Prof. Gronenborn holding the Rosalind Franklin Professorship and Chair.

Prior to her move to Pittsburgh, Prof. Gronenborn was a member of the Senior Biomedical Research Service and Chief of the Structural Biology Section at NIDDK, NIH. She received both her undergraduate and Ph.D. degrees from the University of Cologne, Germany. After post-doctoral training she joined the Scientific Staff in the Divisions of Molecular Pharmacology and Physical Biochemistry at

the National Institute for Medical Research, Mill Hill, London. In 1984, she moved to the Max-Planck Institute in Munich as head of the Biological NMR Group, and in 1988 to the NIH.

Prof. Gronenborn's research harnesses the power of NMR in two major areas: understanding biochemical mechanisms and the structural basis of cellular regulation as well as HIV pathogenesis. She has authored more than 450 publications, including structural studies on interleukins, chemokines, the tumor suppressor protein p53, various transcription factors and enzymes, and a number of HIV-encoded and -associated proteins. She also is noted for her contributions to advancing technology on how best to apply NMR to elucidate important problems in the biosciences.

TECHNOLOGY FORUM - 5:30 PM

Dr. Nathan Clark, University of Pittsburgh

"DNA Sequence Evolution: Resurrecting the Past to See the Future"



The wealth of diversity between species provides us with a unique window on the forces that shaped the biological world. By studying DNA sequences from these species we are able to reconstruct the relationships between them and reveal the functions of their genes. Here, we will review techniques of DNA sequence analysis and their application to pinpoint evolutionary adaptations that allow each species to survive in its environment. We will visit genetic adaptations that combat harmful pathogens and others that allow competition between them. Furthermore, analysis of Neanderthal and Denisovan DNA has revealed that evolutionary adaptations continued to occur relatively recently in our own evolutionary trajectory. In a separate application, our novel analysis technique, evolutionary rate covariation, allows us to computationally predict relationships between genes so that we can piece together the genetic networks that compose all organisms. We demonstrate how rate covariation has been successfully employed to discover new genes in medical genetics, thereby revealing the genetic basis of disease.

Dr. Nathan Clark's work brings computational analysis together with experimental biology in order to understand how evolution has shaped our genes and the complex networks that they form. Dr. Clark began his scientific career as an organic chemist in the lab of C. Grant Wilson at the University of Texas at Austin. He then joined the newly created Genome Sciences Ph.D. program at the University of Washington where he studied the adaptive evolution of reproductive proteins under the mentorship of Willie Swanson. Dr. Clark went on to become an N.I.H. Ruth Kirschstein post-doctoral fellow at Cornell University where he developed novel computational genomic methods to infer protein function in yeasts, fruit flies, and in humans. Now an Assistant Professor in the Department of Computational and Systems Biology at the University of Pittsburgh, his laboratory continues to use evolutionary analysis to predict functional changes to genes and the proteins they encode.

Dinner Reservations:

Please register on-line at <http://www.ssp-pgh.org/monthly-meeting-rsvp/> to make dinner reservations NO LATER THAN Thursday, February 13, 2014 at noon. Dinner will cost \$10 (\$5 for students) and checks can be made out to the SSP. This month's entrée will be Chicken Picatta. If you have any dietary restrictions, please indicate them when you RSVP.

Parking Instructions:

The Duquesne University Parking Garage is located on Forbes Avenue. Upon entering the garage, receive parking ticket and drive to upper floors. Pick up a parking chit at the dinner or meeting.